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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,230	08/12/1999	HARUKI OKMURA	OKAMURA=2E	2359

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,230	OKMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7-9* is/are allowed.

6)☒ Claim(s) *1-6,11 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

The request filed on 02 July 2004 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/373,230 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment filed on 07 June 2004 is acknowledged and entered. Following the amendment, claims 3 and 11 are amended.

Currently, claims 1-9, 11, and 14-17 are pending and under consideration.

Withdrawal of Objections and Rejections:

The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6 remain rejected, and claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the last Office Action mailed on 05 January 2004.

Applicants argument filed on 07 June 2004 has been fully considered, but is not deemed persuasive for reasons below.

At pages 8-9 of the response, the applicant argues that claim 3 has been amended to clearly define the variant with physicochemical properties (1) to (4) and amino acid sequence, and a variant substantially alters biological activity (3) is not covered by the claim. Applicants further argue that "a sequence variant of SEQ ID NO:2" is clear to a skilled person, and that "it is easy for a skilled person to obtain a variant of a molecule encoded by a DNA", citing the

reference "Recombinant DNA". This argument is not persuasive because, with respect to the limitation of "a sequence variant of SEQ ID NO:2", the issue is not whether a skilled person understands the term "a variant of a molecule", which is a general term, rather, the issue is that the metes and bounds of the present "sequence variant of SEQ ID NO:2" are not clear because the claim does not specify % of sequence identity of the variant and SEQ ID NO:2, nor the upper limitation as to how many amino acid residues in SEQ ID NO:2 may be altered (substitution, deletion, or addition) while retaining said biological activity. The claim, therefore, reads on any functional variant of SEQ ID NO:2 without specific sequence limitation. As such, the metes and bounds of the claim cannot be determined.

Claim 11 is indefinite for the following reasons. The claim first recites "a purified ... protein, also known as IGIF and IL-18", and then it states, in part (4), that it possesses "*a part* (or the whole) of the amino acid sequence of SEQ ID NO:2". If the molecule merely has a part of SEQ ID NO:2, it is not an "IGIF" or "IL-18", which, as indicated by applicants, are established terms for molecules with specific sequences. The claimed protein may be a variant or fragment of an IGIF or IL-18.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a specific variant of said protein, which has an amino acid sequence of SEQ ID:2 where residue 70 is methionine or threonine, does not reasonably provide enablement for with claims to variants having physicochemical and functional properties listed in parts (1) to (4) of claim 3, and having the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID:2 replaced with different amino acid, or at least one amino acid residue deleted or added to the N-terminus of SEQ ID:2 while not substantially altering physicochemical properties of the protein. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the previous Office Actions.

Applicants argument on 07 June 2004 has been fully considered, but is not deemed persuasive for reasons below.

At pages 12-13 of the response, the applicant repeatedly argues that it would have been easy for a skilled person to obtain "a sequence variant of SEQ ID NO:2" once the sequence of SEQ ID NO:2 is given, and it only requires routine experimentation, that a protein as defined in the rejected claims are encompassed within the category of "IGIF" or "IL-18" which are established technical terms, and have the specified physicochemical properties, and that the present invention is a pioneer invention and should be given relatively wide protection. This argument is not persuasive because, once again, the issue is not whether making a variant of a molecule is routine, rather, the issue is that the present claims, as written, read on *functional equivalent* of the SEQ ID NO:2 as it does not specify the % variation or the upper limit of the number of residues altered, even though some physicochemical properties are required. Further, although the term "IGIF" or "IL-18" is known in the art, the *claimed* "sequence *variant* of SEQ ID NO:2" reads on a functional equivalent, which can be a structurally distinct molecule from SEQ ID NO:2, and thus, the term "IGIF" or "IL-18" is not a meaningful limitation for the claimed variant. With respect to "a pioneer invention", it is a nature of all patentable inventions, and therefore, it is not a criteria to entitle a broader scope that is not supported by the original disclosure.

Claims 1, 2, 11, and 14-17 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a protein with SEQ ID NO:2, wherein residue 70 is methionine or threonine, does not reasonably provide enablement for any IL-18 (claims 1, 2, 16 and 17, for example) or variants with properties listed in these claims (claims 11, 14 and 15, for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the previous Office Actions.

Applicants argument on 07 June 2004 has been fully considered, but is not deemed persuasive for reasons below.

On page 13 of the response, Applicants further argue that claim 11 comprises limitations other than "a mAb specific to a sequence variant of the protein", and that, contrary to the Examiner's statement that the specification does not disclose any antigenic fragment specific to SEQ ID NO:2, the specification states that a protein having the amino acid sequence of SEQ ID NO:2 has "antigenic fragment(s)". This argument is not persuasive because other limitations are not sufficient to clearly define the molecule, i.e., the claim still reads on a functional equivalent of IL-18, which can have the "other" features as claimed and are distinct molecule from IL-18, as the structural limitation in the claim merely requires "a part" of SEQ ID NO:2, or one antigenic fragment, which can be, for example, 2 to 6 amino acids, and easily embedded in a completely different protein with said biological property. With respect to the disclosure that the protein of SEQ ID NO:2 has "antigenic fragment(s)", it is a general statement, which does not identify the sequence of the "antigenic fragment(s)" specific to SEQ ID NO:2. Further, the specification does not disclose whether the antigenic fragments are, in any way, associated with the functional property. Therefore, such limitations are not meaningful as to how to make a functional variant of IL-18, or a commensurate number of the claimed species, and undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 1-6, 11, 14 and 15 remain further rejected, and the new claim 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the previous Office Actions. Applicants provide no argument in the response to address this issue.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 6, 11, and 14-17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper Nos. 4, 7 and 13.

Applicants argument on 07 June 2004 has been fully considered, but is not deemed persuasive for reasons below.

On pages 14-15 of the response, Applicants present the similar argument as that in the previous responses that the claimed protein is distinct over Nakamura's in molecular weight, activity after SDS-PAGE, and purity. This argument is not persuasive because, as addressed extensively in the previous Office Actions (paper Nos. 7 and 13), a subsequent study published by Okamura et al. (the same group of investigators) demonstrates that the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver, "thus IGIF in the serum sample was proved to be the same IGIF as that found in the liver exact ". The existence of merely different physical forms of the same molecule does not render the molecule itself patentably distinct in the absence of evidence to the contrary. With respect to the assertion that the instantly claimed protein retains the same activity after treatment on SDS-PAGE (whereas Nakamura's factor losses the activity after SDS-PAGE), it is not supported by the present disclosure because, as addressed in the previous Office Actions, the biological activity of the claimed protein was demonstrated using "a present purified protein", which was obtained by the protein purification procedure illustrated in Example 1 of the specification, not by that eluted from SDS-PAGE. Therefore, there is no evidence in the specification to support that the presently claimed protein retains the same activity after treatment on SDS-PAGE. With respect to the issue of purity of the molecule, even if Nakamura's factor were less "pure" to a certain extent than that of the present protein, it is, nonetheless, isolated and purified, and such purity does not change the nature of the molecule, nor renders the molecule itself patentably distinct from the claimed protein in the absence of evidence to the contrary.

At page 15 of the response, the applicant further argues that the allowed claims 7 to 9 are too restrictive when the state of the art is taken into account, and that a skilled person can easily

obtain a sequence variant of SEQ ID NO:2 without infringing on a patent right established on claims 7-9. This argument is not persuasive because the issue is not that whether applicants of the present invention deserve the sequence variants of SEQ ID NO:2, rather, the issue is that the present claims, as written, read on functional equivalent of IL-18 of SEQ ID NO:2, and the scope of the claims is beyond the sequence variants of SEQ ID NO:2 with similar functional property, which is not supported by the original disclosure.

Conclusion:

Claims 7-9 are allowable.

Claims 1-6, 11, and 14-17 are rejected.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Dong Jiang, Ph.D.
Patent Examiner
AU1646
8/18/04

JANET ANDRES
PRIMARY EXAMINER